Evaluation of Bone Marrow Examination in Cases of Pancytopenia in Tertiary Health Center in North-West Rajasthan

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ABSTRACT

Introduction: Pancytopenia is a very common consequence of many haematological diseases with extensive differential diagnosis. It is described as the deficiency of all three cellular elements of blood resulting in anemia and leucopenia and thrombocytopenia. The severity and underlying pathology determines the management and prognosis. Bone marrow examination is an effective way of evaluating various causes of pancytopenia along with other clinical, haematological findings.

Material and methods: In this prospective study, a total 60 patients presenting with pancytopenia on initial work up requiring bone marrow examination were studied along with their relevant clinical history, examination findings, routine haematological findings.

Results: Among 60 cases studied, age of patients ranged from 1-85 years with slight male predominance. Most common age group involve was 11-30 years. Most of the patients presented with generalised weakness, pallor, fever. Dimorphic anemia was the predominant blood picture. The commonest marrow finding was hypercellularity with megaloblastic erythropoiesis. The commonest cause of pancytopenia was megaloblastic anemia 62.79% followed by sub/aleukemic leukemia 25.57%.

Conclusions: Bone marrow examination can diagnosed majority of cases of pancytopenia along with comprehensive clinical and haematological study. It is also helpful in planning further investigations and management.

Keywords: Bone Marrow Examination, Megaloblastic Anemia, Pancytopenia, Sub/aleukemic Leukemia

INTRODUCTION

Pancytopenia is an important clinicohaematological entity encountered in our day to day clinical practice. Pancytopenia is a triad of findings characterised by reduction in all three major formed elements of blood erythrocytes, leucocytes, platelets below their reference values.[1] It is not a diagnosis in itself but a presentation of some underlying general medical or primary haematological disorder.[2] The mechanism of development of pancytopenias varies from the decrease in haematopoietic cell production as in aplastic anemia, trapping of normal cells in hypertrophied and over reactive reticuloendothelial system as in hypersplenism, ineffective haematopoiesis as in megaloblastosis or replacement of normal bone marrow elements by abnormal or malignant cells.[3] Marrow cellularity and composition differs in relation to cause. The final interpretation requires the integration of clinical findings, peripheral blood film findings, bone marrow aspiration and trephine biopsy microscopic examination findings together with the results of other supplement tests. The present study had been done to evaluate the role of bone marrow microscopic examination in finding various causes of pancytopenia.

MATERIAL AND METHOD

This was a prospective study carried out in department of pathology, Sardar Patel Medical College Bikaner, Rajasthan over a period of 2 years from September 2016 to September 2018. All the newly diagnosed 60 pancytopenic cases, referred for bone marrow microscopic examination during this study period and fulfilling the inclusion critera for haemogram were taken for study. In all cases haemogram was correlated with their peripheral blood smear findings.

Inclusion criteria

In adults

Haemoglobin < 13.5gm/dl in male and < 12 gm/dl in female

Total Leucocytes Count < $4*10^9$/l

Total Platelet Count < $150*10^9$/l

In children

Haemoglobin < 10gm/dl

Total Leucocytes Count < $4*10^9$/l

Total Platelet Count < $100*10^9$/l

Exclusion criteria

1. Patients on myelotoxic chemotherapy and radiotherapy were excluded from study.
2. Follow up cases of leukemia and pregnant women were excluded from study.
3. Patients who had recently received blood transfusion were excluded from study.
4. Patients who had not given consent for bone marrow examination were excluded from study.
5. Already diagnosed cases of pancytopenia who were

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taking treatment, excluded from study.

Relevant medical history and clinical details were collected from each patient. All relevant details and sample was collected after taking consent.

Bone marrow aspiration was done from posterior superior iliac spine using Salah bone marrow aspiration needle. Simultaneously, from same puncture site but from a different plane, bone marrow biopsy was done using Jamshidi needle, taking all aseptic precautions and consent.

Peripheral blood smear and bone marrow aspirate smear were stained by Leishman Stain and trephine biopsy were processed and stained by Haematoxylin and eosin stain. Special stain were applied whenever required.

STATISTICAL ANALYSIS

Microsoft word 2007 and Microsoft office 2007 excel was used to generate tables and data was analysed with the help of frequency, proportion, wherever applicable and the results were compared with the previous similar studies.

RESULTS

A total of 60 patients who presented with pancytopenia and indicated for bone marrow examination during study period were studied. They consisted of 53.33% male cases and 46.67% female cases with male to female ratio 1.14:1. The age of patients ranged from 1year to 85 years with maximum number of cases were seen in age group 11years to 30 years (36.67%).

The commonest presenting complaints and physical findings in pancytopenia cases were shown in table1**.**

The commonest mode of presentation was pallor and generalised weakness, followed by fever and other. Splenomegaly were seen mostly in cases of megaloblastic anemia followed by sub/aleukemic leukemia. Lymphadenopathy was noted in all cases of sub/aleukemic leukemia lymphoblastic type.

The haemoglobin(Hb) values ranged from 2.4gm/dl to 9.5gm/dl, majority of cases 46.67% had Hb range from 6-7.9gm/dl and 31.67% had Hb < 6gm/dl, with lowest Hb value was 2.4gm/dl seen in case of megaloblastic anemia.

The total leucocyte count (TLC) ranged from 1050/mm^3 to 3800/mm^3, majority of cases 70% had TLC between 1000-2999/mm^3 and 30% had TLC between 3000-4000/mm^3, with lowest value 1050/mm^3 was seen in case of aplastic anemia.

The total platelet count (TPLC) ranged from 20,000/mm^3

Presenting Complaints and Physical findings	Number of cases out of total n=60	Percentage (%) of cases
Generalised weakness	58	96.67
Fever	28	46.67
Bleeding Manifestations	11	18.33
Weight Loss	06	10
Pallor	60	100
Dyspnea	03	05
Jaundice	03	05
Splenomegaly	08	13.33
Hepatomegaly	01	1.67
Hepatosplenomegaly	06	10.00
Lymphadenopathy	07	11.67
Bony Pain	02	3.33
Other Pain (Body, Abdomen, chest)	16	26.67

Table-1: Presenting complaints and Physical findings in cases of Pancytopenia.

Morphological features on Bone marrow aspiration microscopic examination	Number of cases out of n=60	Percentage of cases (%)
Normoblastic Erythroid Hyperplasia	12	20.00
Megaloblastic Erythroid Hyperplasia	27	45.00
Normoblastic Bone Marrow (NBM) with megaloblastic features in few erythroid cells	01	01.67
Sub/Aleukemic Leukemia	10	16.67
Acute Promyelocytic Leukemia	01	01.67
Plasma cell dyscrasia	02	03.33
Peripheral blood diluted, with few lymphocytes seen.	01	01.67
Hairy Cell Leukemia	01	01.67
Normoblastic Bone Marrow	05	08.32
Total number of cases	60	100

Table-2: The bone marrow aspiration microscopic examination findings in cases of Pancytopenia

Exact cause of pancytopenia cases	Number of pancytopenia cases out of n=43	Percentage of pancytopenia cases (%)
Megaloblastic Anemia	27	62.79
Sub/Aleukemic Leukemia	11	25.57
Multiple Myeloma	02	04.65
Aplastic Anemia	01	02.33
Hairy Cell Leukemia	01	02.33
Non Hodgkin Lymphoma	01	02.33
Total number of cases	43	100

Table-3: Distribution of exact causes of Pancytopenia cases according to the interpretation of Bone Marrow microscopic examination

Study	Country	Number of cases of pancytopenia	Commonest cause	Second most common cause
Keisu M et al[11] (1990)	Israel and europe	100	Neoplastic diseases and radiation (32%)	Hypoplastic anemia (19%)
Tilak et al[12] (1999)	Chandigarh, India	77	Megaloblastic anemia (68%)	Aplstic anemia (7.70%)
Kumar et al[13] (2001)	India	166	Aplastic anemia (29.5%)	Megaloblastic anemia (22.3%)
Khunger et al[2] (2002)	New Delhi, India	200	Megaloblastic anemia (72%)	Aplastic anemia (14%)
Gayathri and Rao et al[9] (2011)	Karnataka, India	104	Megaloblastic anemia (74.04%)	Aplastic anemia (18.26%)
Jha A et al[4] (2012)	Nepal	102	Hypoplastic anemia (29.05%)	Megaloblastic anemia (23.64%)
Chandra K et al[14] (2014)	India	83	Megaloblastic anemia (25.03%)	Sub/aleukemic leukemia (15.67%)
Bahal D et al[6] (2016)	Deharadun, India	60	Megaloblastic anemia (46.66%)	Sub/aleukemic leukemia (20%)
Mallik et al[15] (2016)	Bihar, India	1318	Megaloblastic anemia (31.9%)	Sub/aleukemic leukemia (30.5%)
Present study	Rajasthan, India	60	Megaloblastic anemia (62.79%)	Sub/aleukemic leukemia (25.57%)

Table-4: Comparision of causes of Pancytopenia in various studies.

to 99,000/mm^3, majority of cases 80% had TPLC between 50,000- 1,00,000/mm^3 and 20% cases had TPLC between 20,000- 49,999/mm^3, with lowest value 20,000/mm^3 seen in case of megaloblastic anemia.

Overall, dimorphic anemia (31.67%) was the predominant blood picture and anisopoikilocytosis was seen in majority of the cases. In all cases, leucopenia and thrombocytopenia was seen.

In megaloblastic anemia, dimorphic anemia was seen in 55.56% of cases followed by macrocytic anemia in 40.74% of cases. Hypersegmented neutrophils were seen in 59.26% cases of megaloblastic anemia.

In sub/aleukemic leukemia, normocytic normochromic anemia was seen in all cases and immature cells blasts were seen in 2 cases of acute lymphoblastic leukemia.

The bone marrow aspiration microscopic examination findings were shown in table-2. Out of 60 cases, in only 30 cases bone marrow biopsy was done.

Out of 60 cases, exact cause of pancytopenia were evaluated on the basis of bone marrow microscopic examination only in 43 cases. This distribution is shown in table-3.

Overall marrow cellularity was evaluated only in 30 cases in which both bone marrow aspiration and biopsy both were available for study. Most of the bone marrow were hypercellular 62.07%, followed by normocellular 34.48% and hypocellular 03.45%.

In megaloblastic anemia, bone marrow was hypercellular in 57.14% cases followed by normocellular marrow 42.86%.

DISCUSSION

Pancytopenia is a common haematological finding with variable clinical presentations. It often creats diagnostic challenge to physician and the knowledge of accurate etiology of this condition is crucial in the management of the patient.[4]

60 cases of pancytopenia were studied regarding age, gender wise distribution, presenting complaints, peripheral smear examination, bone marrow microscopic examination findings and final various causes of pancytopenia were evaluated and the results were compared with previous similar studies done in India and abroad.

Most of the patients were in age group 11-30 years (36.67%) which is comparable to Desalphin M et al[5], Bahal D et al[6], Naniwal P et al[7], Shah P et al[8]. The present study shows a definite male preponderance with male to female ratio 1.14:1 which is comparable with Gayateri and Rao et al[9] (1.2:1), Naniwal P et al[7] (1.15:1).

Out of total 60 cases of pancytopenia, bone marrow aspiration microscopic examination was done in all but only in 30 cases bone marrow trephine biopsy was done. As bone marrow biopsy was not indicated in all.

Exact cause was interpretated only in 43 cases out of 60 cases on bone marrow microscopic evaluation and among them megaloblastic anemia was the most commonest cause of pancytopenia seen in 62.79% cases followed by sub/aleukemic leukemia 25.57%, multiple myeloma 04.65%. Also one case (2.33%) each of aplastic anemia, hairy cell leukemia, non Hodgkin lymphoma were seen.

Among n=17 cases, in which exact of pancytopenia was not analysed on the basis of bone marrow microscopic examination findings, n=12, (20%) cases show normoblastic erythroid hyperplasia as compare to Kumar DB et al[10] (27.08%) and Desalphine M et al[5] (22%) study.

Normoblastic erythroid hyperplasia, which by itself is not the cause of pancytopenia and relationship of erythroid hyperplasia to pancytopenia is uncertain as it required a lot

of correlation with clinical and other laboratory parameters. With other causes a possibility of haemolytic anemia in cases of marrow showing erythroid hyperplasia should be ruled out. N=05 cases show normoblastic bone marrow that means cause of pancytopenia lies in the peripheral destruction of blood elements not in bone marrow.

Comparision of causes of pancytopenia in various studies is shown in table 4.

Most studies conducted in India have also reported megaloblastic anemia as a major cause of pancytopenia similar to this study. Higher incidence of megaloblastic anemia in Indian subcontinent can be attributed to low socioeconomic status, poor hygiene, inadequate nutrition and some cultural taboos.

The higher incidence of sub/aleukemic leukemia and multiple myeloma in this study can be attributed to the inclusion of referred and high risk cases in the study, as the study center is a tertiary care hospital with well established cancer hospital and laboratory.

The wide variation in incidence of causes of pancytopenia in different studies published from India as well as other countries can be attributed to the differences in methodology, selection of diagnostic criteria, nutritional status, prevalence of infective disorders and genetic differences in the population as well as varying exposure to myelotoxic agents. Although, the haematological parameters were usually nonspecific in many cases and show a considerable overlap, they do give a diagnostic clues for the evaluation of cases of pancytopenia. Results are almost comparable with Gayateri and Rao et al.[9]

Predominant blood picture was dimorphic anemia 31.67% and hypersegmented neutrophil were seen in 59.26% cases on peripheral blood smear are comparable to Gayateri and Rao et al.[9]

The commonest physical findings were pallor (100%), generalised weakness (96.67%), fever (46.67%), splenomegaly (13.33%), lymphadenopathy (11.67%).

Similar clinical findings have been reported in other studies, although their frequency varies. The differences in the frequency of clinical features can be attributed to geographic variations, genetic make up of the patients and the haematological parameter being predominantly affected in pancytopenia cases.

As the reliability of bone marrow biopsy in assessing cellularity of bone marrow is more than bone marrow aspiration, marrow cellularity was evaluated only in cases where bone marrow aspiration and biopsy both were available after comparing them. There is variation in results regarding marrow cellularity in different studies, as bone marrow cellularity depends upon cause of pancytopenia and extend of bone marrow involvement by that cause.

CONCLUSION

The present study concludes that bone marrow microscopic examination is helpful in understanding of the underlying disease process and in diagnosing the various causes of pancytopenia in majority of cases, along with comprehensive clinical and haematological investigations findings. It is also helpful in planning further investigations and management of pancytopenic cases.

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